among positions 58-69 of the amino acid sequence of human TSH β subunit as depicted in Figure 2 (SEQ ID NO:2).

A3 Cont'd

31. (Amended) the mutant TSH heterodimer of claim 27 which is a mutant of a human TSH heterodimer.

A4

39. (Amended) The mutant TSH heterodimer of claim 27 wherein the hormonal half life in circulation in vivo of the mutant TSH heterodimer is greater than the wild type TSH.

Please add the following new claims:

A5

--67. (New) The mutant TSH heterodimer of claim 28 which is a mutant of a human TSH heterodimer.

68. (New) The mutant TSH heterodimer of claim 28 wherein the hormonal half life in circulation in vivo of the mutant TSH heterodimer is greater than the wild type TSH.--

**REMARKS**

The specification has been amended to correct the priority information. In particular, the specification has been amended to correct the filing date of the provisional, which was inadvertently mistyped in the original specification. Claims 27 and 28 have been amended to incorporate the recitations of Claim 26 and place these claims in independent form. Claims 30, 31, and 39 have been amended to change the dependencies. New Claims 67 and 68 are based on original Claims 31 and 39 respectively. Accordingly, no question of new matter arises and entry of the amendments is respectfully requested.

Claims 27-31, 39, 62, 67, and 68 are before the Examiner for consideration.

## Formal Matter

On page 2 of the Office Action, the Examiner notes that in the continuing data in the first paragraph of the specification, the filing date of the provisional does not match the date on the Declaration. Additionally, the Examiner states that the status of non-provisional parent applications (i.e., whether they are patented or abandoned) should also be included.

In response, Applicants have amended the specification to correct the filing date of the provisional application. In addition, Applicants have amended the specification to recite the status of the non-provisional parent application. Applicants respectfully submit that priority is now perfected.

## Claim Objections

On page 2 of the Office Action, Claims 63, 64, and 66 are objected to as being dependent on non-elected claims. Applicants have cancelled Claims 63, 64, and 66, thereby rendering this objection moot.

## Rejection under 35 U.S.C. §112, first paragraph

On pages 2-3 of the Office Action, Claims 26, 31, 39, 58, 61, 63, 64, and 66 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. In particular, the Examiner states that although the specification is enabled for TSH heterodimers with mutations in specific regions of the α and β subunit, it does not provide reasonable enablement for any other TSH mutants. Also, the Examiner asserts that it would constitute undue experimentation to make and use the invention commensurate in scope with the claims.

Applicants have cancelled Claims 26, 58, 61, 63, 64, and 66, thereby rendering the rejection of these claims moot. With respect to Claims 31 and 39, Applicants have amended these claims to depend on Claims 27, which, as amended, include specific positions for mutations on the TSH α and TSH β subunit. As such, Applicants submit that amended Claims 31 and 39 are fully enabled by the current specification. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

**Rejection under 35 U.S.C. §103(a)**

On pages 3-4 of the Office Action, Claims 27-30 and 62 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Grossman in view of Szkudlinski. Applicants respectfully traverse this rejection in view of the following remarks.

In response to this rejection, Applicants submit herewith two Declarations pursuant to In re Katz, 687 F.2d 450, 215 U.S.P.Q. 14 (CCPA 1982) and MPEP §2132.01. As set forth in the attached Declarations, the relevant portions of each of the cited references originated from the Applicants of the present application. According to MPEP §2132.01, an applicant's disclosure of his or her own work within a year before the filing date cannot be used against him or her under 35 U.S.C. §102(a). Because the cited references were published within one year before the filing date of the present application, and the work set forth in the publications is the work of the inventors, Applicants respectfully request that the cited references be removed from this rejection.

In view of the above, Applicants submit that the present invention is not anticipated by, or obvious over, Grossman alone or in combination with Szkudlinski and respectfully request that the Examiner reconsider and withdraw this rejection.

## CONCLUSION

In light of the above, Applicants believe that this application is now in condition for allowance and therefore request favorable consideration.

If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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SERIAL NO. 09/519,728

DOCKET NO.: 9528-002-27

**MARKED-UP COPY OF PARAGRAPHS, AS AMENDED**

**Replacement for the first paragraph after "Related Applications", at page 1, lines 6-8:**

--This application is a continuation of International Application No. PCT/US98/19772 having an international filing date of September 22, 1998 (abandoned), and claims priority from U.S. [provisional] Provisional Application No. 60/135,505, filed [September 17, 1998] September 22, 1997 (abandoned).--

SERIAL NO. 09/519,728

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**MARKED-UP COPY OF AMENDED CLAIMS**

27. (Amended) A mutant TSH heterodimer comprising (a) a TSH β subunit joined via a peptide bond at its carboxyl terminus to the amino terminus of the carboxyl terminal extension peptide of human chorionic gonadotropin; and (b) an α subunit, wherein at least the TSH β subunit or the TSH α subunit contains at least one amino acid substitution;

wherein the bioactivity of the mutant TSH heterodimer is greater than the bioactivity of wild type TSH heterodimer; and

wherein the at least one amino acid substitution is in amino acid residues selected from among positions 11-21 of the amino acid sequence of human α subunit as depicted in Figure 1 (SEQ ID NO:1).

28. (Amended) A mutant TSH heterodimer comprising (a) a TSH β subunit joined via a peptide bond at its carboxyl terminus to the amino terminus of the carboxyl terminal extension peptide of human chorionic gonadotropin; and (b) an α subunit, wherein at least the TSH β subunit or the TSH α subunit contains at least one amino acid substitution;

wherein the bioactivity of the mutant TSH heterodimer is greater than the bioactivity of wild type TSH heterodimer; and

wherein the at least one amino acid substitution is in amino acid residues selected from among positions 58-69 of the amino acid sequence of TSH β subunit as depicted in Figure 2 (SEQ ID NO:2).

30. (Amended) the mutant TSH heterodimer of claim [26] 27 comprising a mutant human α subunit and a mutant human TSH β mutant subunit, [wherein the mutant human α subunit comprises at least one amino acid substitution in amino acid residues selected from among positions 11-22 of the amino acid sequence of human α subunit as depicted in Figure 1 (SEQ ID NO:1), and] wherein the mutant human TSH β subunit comprises at least one amino acid substitution in amino acid residues selected from among positions 58-69 of the amino acid sequence of human TSH β subunit as depicted in Figure 2 (SEQ ID NO:2).

31. (Amended) the mutant TSH heterodimer of claim [26] 27 which is a mutant of a human TSH heterodimer.

39. (Amended) The mutant TSH heterodimer of claim [26] 27 wherein the hormonal half life in circulation in vivo of the mutant TSH heterodimer is greater than the wild type TSH.